CACATCCGTGTGAATGAAAAGGATGTGCTAATCAGCAAATCTTCCATCAACTTTACT GTCAACTGCAGCTGGTTCAGCGACACCAACGGAGCGGTTGGGTACTTTGCTGTGGTG GTGAGAGAGCCGACAGCATGGATGAGTTGAAGCCAGAACAGCAGCACCCTCTCCC TTCCTACCTGGAGTACAGACACACGCCTCCATCCGAGTCTACCAGACCAATTATTT TGCCAGCAAATGTGCTGAAAGTCCCGACAGCAGTTCTAAAAGTTTCAACATTAAGCT TGGAGCAGAGATGGACAGCCTCGGTGGCAAATGTGATCCCAGTCAGCAGAAATTCT GTGATGGACCGCTGTTGCCACACACCGCCTACAGAATCAGCATCCGGGCTTTTACAC AGCTATTTGACGAGGACTTGAAAGAGTTCACCAAACCTCTCTACTCGGATACGTTCT TCTCTATGCCCATCACCACAGAGTCAGAGCCCTTGTTTGGAGTTATTGAAGGTGTGA GTGCTGGCCTGTTTCTAATTGGCATGCTGGTGGCCCTTGTTGCCTTCTTCATCTGCAG ACAGAAAGCTAGCCACAGCAGGGAAAGGCCATCTGCCCGGCTCAGCATTCGTAGGG ACCGGCCTTTGTCTGTCCATCTGAATCTGGGCCAGAAAGGCAACCGGAAAACTTCTT AACTACCTTCTATCCAAGGAATATGAGGACTTAAAAGACGTGGGTAGAAGCCAGTC ATGTGACATTGCCTCTTGCCTGAGAATCGAGGGAAAAATCGATACAACAACATATT GCCTTATGATGCCTCAAGAGTGAAGCTCTCGAATGTCGATGACGACCCTTGCTCTGA CTACATCAACGCCAGCTACATCCCCGGTAACAACTTCAGACGAGAATACATCGCCA CTCAGGGACCGCTTCCAGGCACCAAGGATGACTTCTGGAAGATGGCGTGGGAGCAG AACGTTCACAACATCGTCATGGTGACCCAGTGTGTTGAAAAGGGCCGAGTGAAGTG TGACCATTACTGGCCAGCAGACCAGGACCCCCTCTACTACGGTGATCTCATCCTACA GATGGTCTCGGAGTCCGTGCTCCCCGAGTGGACCATCAGGGAGTTTAAGATATGCAG TGAAGACAGTTGGATGCACACAGACTCATCCGTCACTTTCACTACACGGTGTGGCC AGACCATGGGGTCCCAGAGACCACCCAGTCCCTGATCCAATTTGTGAGGACAGTCA GGGACTACATCAACAGAAGCCCCGGGGCTGGGCCCTCCGTAGTGCACTGCAGCGCT GGTGTGGGCAGAACAGGGACGTTCGTTGCCCTGGACCGGATCCTCCAGCAGTTGGA CTCTAAGGACTCCGTGGACATTTATGGGGCAGTGCATGACCTAAGACTCCACAGGGT TCACATGGTCCAGACCGAGTGTCAATATGTGTATCTGCATCAGTGTGTAAGAGACGT CTCAGAGCAAAGAACTGCGGAAACGAGCAAGAGAAAGGGGGTGTTTCGATTTATG AGAATGTGAATCAGAGTATCACAGAGATGCAATCTACTCGAGACATTAAGAATTC (SEQ ID NO:1)

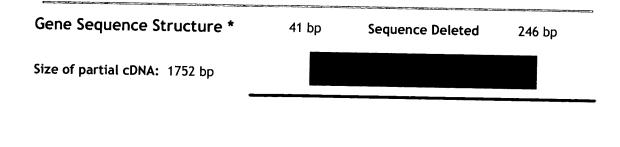
FIGURE 1

<u>underlined</u> = deleted in targeting construct

[] = sequence flanking Neo insert in targeting construct

[GTCAAGGAAGAGGTACCTGGTGTCCATCAAGGTGCAGTCG]GCCGGCATGACCAGTGAGGT GGTTGAAGATAGCACCATCACCATGATAGACCGCCCCGCCTCAACCGCCTCCACACATCCG TGTGAATGAAAAGGATGTGCTAATCAGCAAATCTTCCATCAACTTTACTGTCAACTGCAG CTGGTTCAGCGACCCAACGGAGCGGTTGGGTACTTTGCTGTGGTGGTGAGAGAGGCCGA CAGCAT [GGATGAGTTGAAGCCAGAACAGCAGCACCCTCTCCCTTCCTACCTGGAGTACAG ACACAACGCCTCCATCCGAGTCTACCAGACCAATTATTTTGCCAGCAAATGTGCTGAAAG TCCCGACAGCAGTTCTAAAAGTTTCAACATTAAGCTTGGAGCAGAGATGGACAGCCTCGG TGGCAAATGTGATCCCAGTCAGCAGAAATTCTGTGATGGACCGCTGTTGCCACACACCGC CTACAG] AATCAGCATCCGGGCTTTTACACAGCTATTTGACGAGGACTTGAAAGAGTTCAC CAAACCTCTCTACTCGGATACGTTCTTCTCTATGCCCATCACCACAGAGTCAGAGCCCTT GTTTGGAGTTATTGAAGGTGTGAGTGCTGGCCTGTTTCTAATTGGCATGCTGGTGGCCCT TGTTGCCTTCTTCATCTGCAGACAGAAAGCTAGCCACAGCAGGGAAAGGCCATCTGCCCG GCTCAGCATTCGTAGGGACCGGCCTTTGTCTGTCCATCTGAATCTGGGCCAGAAAGGCAA CCGGAAAACTTCTTGCCCCATAAAGATCAATCAGTTTGAAGGGCATTTCATGAAGCTGCA GGCAGACTCCAACTACCTTCTATCCAAGGAATATGAGGACTTAAAAGACGTGGGTAGAAG CCAGTCATGTGACATTGCCTCTTGCCTGAGAATCGAGGGAAAAATCGATACAACAT ATTGCCTTATGATGCCTCAAGAGTGAAGCTCTCGAATGTCGATGACGACCCTTGCTCTGA CTACATCAACGCCAGCTACATCCCCGGTAACAACTTCAGACGAGAATACATCGCCACTCA GGGACCGCTTCCAGGCACCAAGGATGACTTCTGGAAGATGGCGTGGGAGCAGAACGTTCA CAACATCGTCATGGTGACCCAGTGTGTTGAAAAGGGCCGAGTGAAGTGTGACCATTACTG GCCAGCAGACCAGGACCCCTCTACTACGGTGATCTCATCCTACAGATGGTCTCGGAGTC CGTGCTCCCCGAGTGGACCATCAGGGAGTTTAAGATATGCAGTGAAGAACAGTTGGATGC ACACAGACTCATCCGTCACTTTCACTACACGGTGTGGCCAGACCATGGGGTCCCAGAGAC CACCCAGTCCCTGATCCAATTTGTGAGGACAGTCAGGGACTACATCAACAGAAGCCCCGG CCTGGACCGGATCCTCCAGCAGTTGGACTCTAAGGACTCCGTGGACATTTATGGGGCAGT GCATGACCTAAGACTCCACAGGGTTCACATGGTCCAGACCGAGTGTCAATATGTGTATCT GCATCAGTGTGTAAGAGACGTCTCAGAGCAAAGAAACTGCGGAAACGAGCAAGAGAAAGG GGGTGTTTCGATTTATGAGAATGTGAATCAGAGTATCACAGAGATGCAATCTACTCGAGA CATTAAGAATTC

FIGURE 2A

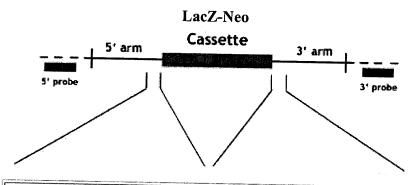


Targeting Vector* (genomic sequence)

Arm Length: 5': 0.7 kb 3': 2.5 kb

Targeting Vector Endogenous Locus

* Not drawn to scale



5'>GCCGCCCCAGAACTCCACGG CCATTGCCTGCTCTTGGATACCTC CTGACTCCGACTTTGATGGCTACA GCATTGAGTGCCGAAAAATGGATA CCCAAGAAATCGAGTTTTCCAGAA AGCTGGAGAAAGAAAATCACTGC TCAACATCATGATGTTAGTACCTC ATAAGAGGTACCTGGTGTCCATCA AGGTGCAGTCG<3 '

(SEQ ID NO:2)

5'>GGATGAGTTGAAGCCAGAACA GCAGCACCCTCTCCCTTCCTACCT GGAGTACAGACACACGCCTCCAT CCGAGTCTACCAGACCAATTATTT TGCCAGCAAATGTGCTGAAAGTCC CGACAGCAGTTCTAAAAGTTTCAA CATTAAGCTTGGAGCAGAGATGGA CAGCCTCGGTGGCAAATGTGATCC CAGTCAGCAGA<3' (SEQ ID NO:3)

FIGURE 2B